

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appellant: Donald L. Wise, Debra J. Trantolo, David D. Hile, and Stephen A. Doherty

Serial No.: 10/613,975 Art Unit: 1645

Filed: July 3, 2003 Examiner: Khatol Shahnan-Shah

For: *VACCINES TO INDUCE MUCOSAL IMMUNITY*

Mail Stop Appeal Brief-Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPEAL BRIEF

Sir:

Appellants have requested reinstatement of the Appeal filed February 22, 2006. With only very minor differences, the same issues are present in the office action rejecting claims 1 and 3-11 mailed August 7, 2006, in the above-identified patent application. A Notice of Appeal was re-filed on November 11, 2006. The Commissioner was originally authorized to charge the fee for filing the Appeal Brief for a large entity, to Deposit Account No. 50-3129, February 22, 2006, so no additional fee should be required. However, should a fee be required, the Commissioner is hereby authorized to charge the fee to Deposit Account No. 50-3129.

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(1) REAL PARTY IN INTEREST

The real party in interest of this application is Depuy Mitek, a Johnson & Johnson company.

(2) RELATED APPEALS AND INTERFERENCES

There are no related appeals or interferences known to appellant, the undersigned, or appellant's assignee which directly affects, which would be directly affected by, or which would have a bearing on the Board's decision in this appeal.

(3) STATUS OF CLAIMS

Claims 1 and 3-11 are pending and on appeal. Claims 2 and 12-21 have been cancelled. The text of each claim on appeal, as pending, is set forth in an Appendix to this Appeal Brief.

It appears the examiner is confused with regard to the status of claim 2. As was corrected noted in the Office Action mailed November 3, 2004, claim 2 was cancelled and claim 3 was amended. See also the Amendment mailed August 10, 2004, page 2. It may be that the record is in error.

(4) STATUS OF AMENDMENTS

The claims were last amended in an amendment filed on January 4, 2007, in response to the office action mailed on August 7, 2006. In a telephone call with the examiner on January 8, 2007, the examiner indicated that this amendment would be entered.

(5) SUMMARY OF CLAIMED SUBJECT MATTER

Independent claim 1 defines a vaccine composition for inducing an immune response to a pathogen comprising a nucleic acid encoding an antigen eliciting an immune response to the

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pathogen encapsulated in a mucoadhesive controlled release particulate formulation comprising an open-celled polymeric foam of approximately 95% void volume, or particles thereof. Support for claim 1 can be found in the specification at least at page 8, lines 5-6, 16-18 and 20; at page 11, lines 1-2; page 20, lines 10-11; page 10, lines 26-27; page 25, lines 17-20 and claim 1 as originally filed. As defined by claim 3 the composition comprises a mucoadhesive polymer coating (see at least page 25, lines 17-20). As defined by claim 4, the composition comprises an enteric outer coating or capsule (see at least page 20, lines 28-31).

As defined by claim 5, the composition has a particulate diameter of less than five microns (see at least page 8, lines 12-13). Claim 8 defines the polymer as a low molecular weight poly(D,L-lactide-co-glycolide) (see at least page 8, lines 3-5).

Claim 9 defines the pathogens as selected from the group consisting of *Plasmodium falciparum*, *Francisella tularensis*, *Bacillus anthracis*, and *Helicobacter pylori* (see page 7, lines 9-12). Claim 10 defines the composition as also containing an adjuvant (see at least page 23, lines 9-10). Claim 11 defines the antigen as expressed or released for a period of weeks to months (see at least page 8, lines 13-16).

As defined by claim 6 the composition is formed by lyophilizing a solution of a biodegradable polymer to form an open-celled polymeric foam of approximately 95% void volume (see at least page 8, lines 5-6), impregnating the foam with an aqueous solution of the nucleic acid (see at least page 8, lines 6-7, lyophilizing the foam to remove the water (see at least page 8, lines 7-8, and extruding the resulting matrix at ultrahigh pressures (see at least page 8, line 8). As defined by claim 7, the method also contains the step of cryogenically grinding the

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matrix to an average particle size of fifteen microns in diameter; and sieving to isolate particles less than five microns in diameter (see at least page 8, lines 10-13).

(6) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues presented on appeal are:

(1) whether claims 1 and 3-11 are enabled as required by 35 U.S.C. § 112, first paragraph.

(2) whether claims 1 and 3-11 satisfy the written description requirement as required by 35 U.S.C. § 112, first paragraph.

(3) whether claim 9 is definite as required by 35 U.S.C. § 112, second paragraph.

(4) whether claims 1, 3-5 and 8-11 are anticipated by O'Hogen. *J. Pharm. Pharmacol.*, 50(1):1-10 (1998) ("O'Hogan")

(5) whether claims 1, 3-5, and 8 are anticipated by Perez, et al., *J. Control Release*, 75:211-224 (2001) ("Perez").

(7) ARGUMENT

(A) The Invention

Mucous membranes are the primary routes of entry for a large number and wide variety of disease carrying agents. Many pathogens enter and replicate at the mucosal surface before causing systemic infection. The mucosal immune system can be stimulated by oral administration. However, the induction of mucosal immunity has been shown to depend on a number of variables including the delivery system. Local administration of antigens usually requires large amounts of antigen to produce a response (see at least page 9). At stated at page 9,

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of the specification, delivery of antigen is key to developing an immune response and that under-stimulation may fail to prime the immune system. The present application relates to the development of effective and long-lasting vaccines, especially vaccines incorporating nucleic acid encoding antigen, such as plasmid DNA, by encapsulating the DNA within a mucoadhesive controlled release particulate formulation.

As discussed at least at page 17, administration of naked DNA leaves the vaccine vulnerable to attack by enzymes that can reduce the half-life to minutes or hours. Chemical modification can increase the half life of the vaccines, but this may also increase systemic toxicity. Vaccines, including DNA vaccines, have been widely available for a long time. However, no one has put them into a mucoadhesive controlled release particulate formulation, as claimed herein. As discussed at least at page 8, the mucoadhesive controlled release particulate formulation protects the antigen and stimulates and maintains the immune response to pathogens.

(B) Rejections under 35 U.S.C. § 112, first paragraph, enablement

Claims 1 and 3-11 were rejected as non-enabled.

The Legal Standard for Enablement

The Court of Appeals for the Federal Circuit (CAFC) has described the legal standard for enablement under 35 U.S.C. § 112, first paragraph, as whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art without undue experimentation. See, e.g., *Amgen v. Hoechst Marion Roussell* 314 F.3d 1313 (Fed. Cir. 2003) and *Genentech, Inc. v. Novo Nordisk A/S*, 108 F3d at 165, 42 USPQ2d at

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1004 (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). See also *In re Fisher*, 427 F.2d at 839, 166 USPQ at 24; *United States v. Teletronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); and *In re Stephens*, 529 F.2d 1343 (CCPA 1976). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *M.I.T. v. A.B. Fortia*, 774 F.2d 1104 (Fed. Cir. 1985). In addition, as affirmed by the Court in *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524 (Fed. Cir. 1987), a patent need not teach, and preferably omits, what is well known in the art.

Whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See *In re Wands*, 858 F.2d 731, 735, 736-737, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in *Wands*, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. In cases that involve unpredictable factors, "the scope of the enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.' *In re Atlas Powder Co., v. E.I. DuPont De Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984).

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As noted in *Ex parte Jackson*, the test is not merely quantitative, since a considerable amount of experiment is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed. See *Ex parte Jackson*, 217 USPQ 804, 807 (PTO Bd. App. 1982). The adequacy of a specification's description is not necessarily defeated by the need for some experimentation to determine the properties of a claimed product. See *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F3d 956, 965-966 63 USPQ2d 1609, 1614 (Fed. Cir. 2002). There is no requirement for examples.

As the Board of Patent Appeals stating,

"Nevertheless, "[w]hen rejecting a claim under the enablement requirement of section 112," it is well settled that "the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the